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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,389	12/18/2001	Georges Natsoulis	0800-0005.04	1714

7590

02/06/2003

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EXAMINER

MARVICH, MARIA

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 02/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/026,389

Applicant(s)

NATSOULIS ET AL.

Examiner

Maria B Marvich, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 November 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2-4, 8, 9, 13, 15 and 16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-4, 8, 9, 13, 15 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This office action is in response to an amendment filed 11/25/02. Claims 1, 5-7, 10-12 and 14 have been cancelled. Claims 2-4, 8, 9, 13, 15 and 16 are pending in this application.

#### ***Priority***

The instant application claims by way of priority the following- continuation of 09/449,581 (now US 6,365,403), which is a continuation of 09/107,708 (now US 6,027,931), which is a continuation-in-part of 08/688,648, which is a continuation-in-part of 08/510,790 (now US 5,622,856). Priority for the claim language “an accessory function vector” cannot be supported by applications 08/510,790 (now US patent 5,622,856) and 08/688,648. Therefore, priority for this limitation is set at 6/30/98.

#### ***Response to Arguments***

Rejection of claims 1, 3-7, 9-12, 14 and 16 under 35 U.S.C. 101, statutory double patenting has been withdrawn in light of amendments to claims.

Rejection of claims 2, 8, 12, 13, 14 and 15 under 35 U.S.C. 101, non-statutory double patenting has been withdrawn in light of amendments to claims.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for

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patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2-4, 8, 9, 13, 15 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Shenk et al. (US 5,436,146).

Shenk et al. teach stocks of recombinant adeno-associated adenovirus (rAAV) that are free of adenovirus and herpes virus. While the rAAV of Shenk et al is produced by slightly different methods from that of the instant application; the resulting product, absent evidence to the contrary, does not differ from that in Shenk et al (see MPEP 2113 and response to argument below).

Claims 2-4, 8, 9, 13, 15 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Colosi et al. (US 6,004,797, filing date 11/9/1995).

Colosi et al. disclose adenovirus helper-free rAAV production. Accessory functions are provided for AAV production by plasmids and not by adenovirus or herpes virus. rAAV were produced using transfection to supply accessory functions that were devoid of contaminating helper virus (table 1, column 21).

Claims 2-4, 8, 9, 13, 15 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Xiao et al. (Journal of Virology, March 1998 Vol. 72(3), pp 2224-2232).

Xiao et al. disclose rAAV virions that are completely free of adenovirus helper virus (abstract). The helper functions are delivered from a plasmid, pXX6 that contains the essential helper genes but lacks the Ad structural and replication genes. In combination with pXX2, a

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novel AAV packaging construct, yields of rAAV are increased 40 fold (page 2225, column 1 last paragraph through first paragraph, column 2).

### ***Response to Arguments***

Applicants traverse the claim rejections under 35 U.S.C. 102(e) on page 8 of the response filed 11/25/02. Applicant argues that Shenk et al. fails to anticipate the instant claims in that the instant claims are directed to stocks recombinant AAV virions produced using accessory function vectors and therefore, the resultant stock is free from infectious viral particles such as adenovirus and herpes virus.

Applicant's arguments filed 11/25/02 have been fully considered but they are not persuasive. The patentability of the instant invention, which while defined by the process, is based upon the product (see MPEP 2113). The stock of recombinant AAV of the instant invention are produced so to reach high titers by manipulation of the expression of the long and short rep proteins such that the toxic long rep proteins are under expressed in comparison to the short rep protein. The method further involves an accessory function vector, which includes (page 14, line 14-20) nucleotide sequences providing accessory functions and expressly excludes infectious particles. The inclusion of these steps does not alter the end product from that resulting from the 5,436,146 patent. Shenk et al. teach a recombinant AAV stock produced by a different method. However, the stock is generated by producing a cell lysate in which the helper virus is then heat inactivated and the rAAV virions are then purified from other elements of the cell lysate by for example ultracentrifugation in a cesium chloride gradient (column 13, line 5-12).

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Therefore, Shenk et al. anticipated the instant invention by teaching stocks of recombinant AAV virions that are free of helper virus.

Claims 2-4, 8, 9, 13, 15 and 16 are rejected.

### *Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (703) 305-1998. The fax phone numbers for

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the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3291.

Maria B Marvich, PhD  
Examiner  
Art Unit 1636

February 5, 2003

DAVID GUZO  
PRIMARY EXAMINER  
